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EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,185	FRANC ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/28/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-7 are currently pending.

Priority

The instant application is a 371 of PCT/CZ04/00078 filed on 11/23/2004 and claims benefit of foreign applications filed on 11/25/2003. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). A certified copy of foreign application has been submitted on 5/22/2006.

The earliest effective U.S. filing date afforded the instantly claimed invention has been determined to be 11/23/2004.

Information Disclosure Statement (IDS)

A signed and initialed copy of the IDS papers filed on 5/28/2009 is enclosed in this action.

WO 2004/006937 is not considered. Although it contains English abstract, Applicant did not provide a concise explanation of relevance and did not include the statement that the abstract is the only portion which caused it to be listed and the other portion is not relevant.

Each information disclosure statement must further include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information listed that is not in the English language.

The concise explanation may be either separate from the specification or part of the specification. If the concise explanation is part of the specification, the IDS listing should include the page(s) or line(s) numbers where the concise explanation is located in the specification.

The requirement for a concise explanation of relevance is limited to information that is not in the English language. The explanation required is limited to the relevance as understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information at the time the information is submitted to the Office. If a complete translation of the information into English is submitted with the non-English language information, no concise explanation is required. An English-language equivalent application may be submitted to fulfill this requirement if it is, in fact, a translation of a foreign language application being listed in an information disclosure statement. There is no requirement for the translation to be verified. Submission of an English language abstract of a reference may fulfill the requirement for a concise explanation. Where the information listed is not in the English language, but was cited in a search report or other action by a foreign patent office in a counterpart foreign application, the requirement for a concise explanation of relevance can be satisfied by submitting an English-language version of the search report or action which indicates the degree of relevance found by the foreign office. This may be an explanation of which portion of the reference is particularly relevant, to which claims it applies, or merely an "X", "Y", or "A" indication on a search report. The requirement for a concise explanation of non-English language information would not be satisfied by a statement that a reference was cited in the prosecution of a United States application which is not relied on under 35 U.S.C. 120.No information disclosure statement has been filed.

Claim Objections

Claims 3 and 5 are objected because of the following informalities: typographical errors. The term "are" in line 5 of claim 3 should be corrected to --is--. Also, the term "spraing" in line 2 of claim 5 should be corrected to --spraying--.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All the dependent claims are included.

Claim 1 recites the following limitation: "the obtained aqueous suspension is sprayed in a fluid bed onto a solid particle hydrophilic carrier having such distribution of particle size that the size of 90% of particles exceeds 40 μm and the size of 10% of particles exceeds 200 μm and the size of 99% of particles does not exceed 300 μm". It is unclear whether "particle" or "particles" refers to the "solid particle hydrophilic carrier" or the resulting final product. Claims 2-7 are included because they are dependent from claim 1 thus incorporate its limitation. For the examination purpose, it is interpreted as referring to the "solid particle hydrophilic carrier".

Regarding claims 3-5 and 7, the phrases "particularly" in line 3 of claim 3 and 7 and "such as" in line 5 of claims 4-5 renders the claims indefinite because it is unclear whether the

limitation following the phrase is part of the claimed invention. Also, the recitation "a hydrophilic sugar, as sucrose……" in line of claim 3 is construed to mean "a hydrophilic sugar, such as sucrose……", it is also unclear whether the limitation following the phrase is part of the claimed invention.

Claim 6 recites "optionally after being mixed with at least one lubricant and/or with at least one disintegrant". Since it is optional and alternative recitation "or" is used, the method of claim 6 may or may not have a step of mixing with both lubricant and disintegrant or either one. However, claim 5 requires the step of mixing with both lubricant and disintegrant, thus claim 6 recites the broader limitation than claim 5, which claim 6 is dependent from. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being obvious over US patent 5,145,684 (issue date: 9/8/1992) in view of US patent 6,294,192 (issue date: 9/25/2001) and US patent 5,464,612 (issue Date: 9/25/2001).

US patent 5,145,684 teaches a method of preparing stable and dispersible drug nanoparticles by wet milling in the presence of grinding media in conjunction with a surface modifier (surfactant), wherein the drug substance is poorly soluble and dispersible in at least one liquid medium and a preferred surface modifier is anionic surfactant such as sodium dodecylsulfate (sodium lauryl sulfate) (column 3, lines 16-24, column 3, lines 40-52, and column 4, lines 34-63). It further disclosed that the particles are prepared in a method comprising the steps of dispersing a drug substance in a liquid dispersion medium such as water (aqueous solution) applying mechanical means such as milling in the presence of surface modifier to reduce the particle size, wherein the concentration of the drug substance in the liquid medium can vary from about 0.1-60%, and preferably is from 5-30% (w/w) and the surface modifier is present in the premix and the concentration of the surface modifier can vary from about 0.1 to about 90%, and preferably is 1-75%, more preferably 20-60%, by weight based on the total combined weight of the drug substance and surface modifier (column 5, lines 41-47, and column 5, line 62-column 6, line 4). It also discloses that the dispersion of surface modified drug nanoparticles can be spray-coated onto sugar spheres (hydrophilic carrier) or onto a pharmaceutical excipient in a fluid-bed spray coater by techniques well known in the art (column 7, lines 47-52) and the particles can be made into pharmaceutical compositions for oral administration column 7, lines 53-60). In addition it teaches that more specifically, in accordance with this invention, there are provided particles consisting essentially of a crystalline drug substance having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less than about 400 nm, wherein at least 90% of the particles have average particle size of less than about 400 nm (column 5, lines 20-40). Since 90%

of the particles have average particle size of less than about 400 nm (0. 4 μm), it is considered that the size of 10% of particles does not exceed 2 μm, the size of 50% of particles does not exceed 7 μm. Furthermore, the drug particles of this invention exhibits high bioavailability and provide more rapid onset of drug action (considered as instant release) and decreased gastrointestinal irritancy (column 8, lines 3-9). In the preferable examples, steroid derivatives such as danazol (a modified testosterone) are used as an insoluble drug substance (examples 3-5).

The reference differs from the instant invention insofar as it does not state finasteride as a drug substance in use. In addition, it is silent about the particle size of hydrophilic carrier such as sugar.

US patent 6,294,192 teaches a composition comprising hydrophobic therapeutic agent and a combination of a hydrophilic surfactant such as sodium lauryl sulfate and sodium dioctyl sulfosuccinate and a hydrophobic surfactant, wherein finasteride is listed as a hydrophobic therapeutic agent which has little or no water solubility (abstract, column 21, lines 48-57, claim 42 and column 18, line 13-21).

US patent 5,464,612 discloses the granulation procedure for solid preparation wherein a granulation machine is charged with seed particles such as granulated sugar with an average particle size of about 100 to 300 μm and the powder containing the medicinally active ingredient together with excipients or additives is introduced and caused to adhere to the seed particles (column 5, line 60-column 6, line 5).

It would have been prima facie obvious to one having ordinary skill in the art at the time of the invention was made to apply the method taught by US patent 5,145,684 in the preparation

of the particles of finasteride taught by US patent 6,294,192 because of the following reasons: US patent 5,145,684 teaches a method of preparing nanoparticles by wet milling in the presence of grinding media in conjunction with a surface modifier (surfactant), which can be generally used for insoluble drug substances such as steroid derivatives. US patent 6,294,192 teaches finasteride (steroid derivatives) as insoluble drug. Thus, it would be prima facie obvious to apply the method of US patent 5,145,684 for any insoluble drug substance including finasteride on the expectation that finasteride prepared by the method of US patent 5,145,684 would also exhibits high bioavailability and provide more rapid onset of drug action and decreased gastrointestinal irritancy. With regard to the particle size of hydrophilic carrier recited in claim 1, it would be prima facie obvious to one having ordinary skill in the art at the time of the invention was made to optimize the particle size of a hydrophilic carrier depending on the desired size of the final particles since US patent 6,294,192 discloses the particle size of sugar used as carriers (seeds) for granulation ranges about 100 to 300 μm.

2. Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being obvious over US patent 5,145,684 (Issue date: 9/8/1992) in view of US patent 6,294,192 and US patent 5,464,612 (Issue date: 9/25/2001) and in the further view of Ansel *et al.* (Pharmaceutical Dosage Forms and Drug Delivery Systems, 5th Ed., p92-99 and p161-182, 1990).

US patent 5,145,684 teaches a method of preparing stable and dispersible drug nanoparticles by wet milling in the presence of grinding media in conjunction with a surface modifier (surfactant), wherein the drug substance is poorly soluble and dispersible in at least one liquid medium and a preferred surface modifier is anionic surfactant such as sodium

dodecylsulfate (sodium lauryl sulfate) (column 3, lines 16-24, column 3, lines 40-52, and column 4, lines 34-63). It further disclosed that the particles are prepared in a method comprising the steps of dispersing a drug substance in a liquid dispersion medium such as water (aqueous solution) applying mechanical means such as milling in the presence of surface modifier to reduce the particle size, wherein the concentration of the drug substance in the liquid medium can vary from about 0.1-60%, and preferably is from 5-30% (w/w) and the surface modifier is present in the premix and the concentration of the surface modifier can vary from about 0.1 to about 90%, and preferably is 1-75%, more preferably 20-60%, by weight based on the total combined weight of the drug substance and surface modifier (column 5, lines 41-47, and column 5, line 62-column 6, line 4). It also discloses that the dispersion of surface modified drug nanoparticles can be spray coated onto sugar spheres (hydrophilic carrier) or onto a pharmaceutical excipient in a fluid-bed spray coater by techniques well known in the art (column 7, lines 47-52) and the particles can be made into pharmaceutical compositions for oral administration column 7, lines 53-60). In addition it teaches that more specifically, in accordance with this invention, there are provided particles consisting essentially of a crystalline drug substance having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less than about 400 nm, wherein at least 90% of the particles have average particle size of less than about 400 nm (column 5, lines 20-40). Since 90% of the particles have average particle size of less than about 400 nm (0. 4 μm), it is considered that the size of 10% of particles does not exceed 2 μm, the size of 50% of particles does not exceed 7 μm. Furthermore, the drug particles of this invention exhibits high bioavailability and provide more rapid onset of drug action (considered as instant release) and decreased

gastrointestinal irritancy and (column 8, lines 3-9). In the preferable examples, steroid derivatives such as danazol (a modified testosterone) are used as an insoluble drug substance (examples 3-5).

The reference differs from the instant invention insofar as it does not state finasteride as a drug substance in use. Also, it is silent about the particle size of hydrophilic carrier such as sugar. In addition, it is silent about adding a lubricant and/or a disintegrant for making tablet or capsule and film coating recited in claims 4-7.

US patent 6,294,192 teaches a composition comprising hydrophobic therapeutic agent and a combination of a hydrophilic surfactant such as sodium lauryl sulfate and sodium dioctyl sulfosuccinate and a hydrophobic surfactant, wherein finasteride is listed as a hydrophobic therapeutic agent which has little or no water solubility (abstract, column 21, lines 48-57, claim 42 and column 18, line 13-21).

US patent 5,464,612 discloses the granulation procedure for solid preparation wherein a granulation machine is charged with seed particles such as granulated sugar with an average particle size of about 100 to 300 μm and the powder containing the medicinally active ingredient together with excipients or additives is introduced and caused to adhere to the seed particles (column 5, line 60-column 6, line 5).

Ansel *et al.* teaches a manufacturing practice of pharmaceutical dosage forms and lists disinterant, lubricant, and coating agent as commonly added ingredients in tablet formulation (p94, column 2, last paragraph-p95 column 2, 2nd paragraph and p98, table 4-2). It further disclose that tablet lubricants improve the flow of the granulation, prevent the adhesion of the tablet formulation to the punches and dies, and reduced friction during tablet compression

(antistatic effect) and the quantity of lubricant used varies from one tableting operation to another and may range from 0.1% to 5% (p171, column 2, last paragraph). Also, it teaches that disintergrating agents include starch, polyvinyl polypyrrolidone and crospovidone and the quantity of lubricant usually used is 5% when starch is employed (p167, column 2, last paragraph). In addition, it teaches that tablets are film coated by the application or spraying of the film-coating solution, wherein a typical aqueous film-coating formulation contains 7-18% of film-forming polymer such as hydroxypropyl methylcelluose (p180, column 2, 2nd paragraph and p181, column 1, 2nd paragraph).

It would have been prima facie obvious to one having ordinary skill in the art at the time of the invention was made to apply the method taught by US patent 5,145,684 in the preparation of the particles of finasteride taught by US patent 6,294,192 because of the following reasons: US patent 5,145,684 teaches a method of preparing nanoparticles by wet milling in the presence of grinding media in conjunction with a surface modifier (surfactant), which can be generally used for insoluble drug substances such as steroid derivatives. US patent 6,294,192 teaches finasteride (steroid derivatives) as insoluble drug. Thus, it would be prima facie obvious to apply the method of US patent 5,145,684 for any insoluble drug substance including finasteride on the expectation that finasteride prepared by the method of US patent 5,145,684 would also exhibits high bioavailability and provide more rapid onset of drug action and decreased gastrointestinal irritancy. With regard to the particle size of hydrophilic carrier recited in claim 1, it would be prima facie obvious to one having ordinary skill in the art at the time of the invention was made to optimize the particle size of a hydrophilic carrier depending on the

desired size of the final particles since US patent 6,294,192 discloses the particle size of sugar used as carriers (seeds) for granulation ranges about 100 to 300 μm.

With regard to adding a lubricant and/or a disintegrant for making tablet or capsule and film coating recited in claims 4-7, it would have been prima facie obvious to one having ordinary skill in the art at the time of the invention was made to add steps of mixing with a lubricant and/or a disintegrant in the making tablets or capsules and coating tablets with film coating dispersion to the method taught by US patent 5,145,684 in order to make a solid dosage form such as tablets and capsules since those steps are well-known in the pharmaceutical art and lubricants, disintegrants, and coating agents are commonly used excipients for solid dosages forms as evidenced by Ansel *et al.*

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 8:00-5:00 Monday-Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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